Levels of plasma ACTH in men from infertile couples

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Abstract

INTRODUCTION: Emotional stress connected with work or, for example, depressive reaction to infertility, is one of frequent causes of decreased quality of semen. An objective examination of this factor is difficult because stress depends also on patient's emotionality. One of the ways to study this problem is evaluating the relation between ACTH level and selected semen parameters.
MATERIAL AND METHODS: The study was based on results of the examination of 83 men from couples treated for infertility in the Gynecology and Infertility Clinic of the Jagiellonian University in Krakow. Determination of ACTH, FSH, LH, cortisol, testosterone and androstendion was performed using ELISA
RESULTS: Lower average values of semen volume, sperm cells concentration and A sperm cell mobility and higher value of D sperm cells mobility were identified in the group of men from couples treated for infertility with ACTH level >30pg/ml in comparison to the WHO standards and the control group with ACTH <30pg/ml. Higher ACTH and cortisol levels were detected in the group of men with the sperm count <10mln/mL in comparison to the control group with the sperm count >20mln/mL. Low and statistically insignificant correlation was observed between androstendion and testosterone levels, what might suggest the reduction of testosterone synthesis in this group.
CONCLUSIONS: Our results might indicate that the rise of ACTH and cortisol inhibit the conversion of adrostendion into testosteron in Leydig-cells resulting in the rise of androstendion, drop of testosterone production and lower average

ORIGINAL ARTICLE

Introduction

Emotional stress connected with work or, for example, depressive reaction to infertility, is one of frequent causes of decreased quality of semen. An objective examination of this factor is difficult because stress depends also on patient's emotionality. One of the ways to study this problem is evaluating the relation between ACTH level and selected semen parameters. The highest ACTH level is noted in the morning, while the lowest at midnight. In response to psycho-emotional stimuli the secretion of cortisol via CRH (corticotropin-releasing hormone) and ACTH growths occurs. In danger the suppression of the gonadal axis takes place through suppressive action of CRH on GnRH in two pathways through cortisol and beta-endorphins [3–5]. The drop of GnRH pulsating secretion leads to the decrease of FSH release from the anterior lobe of the hypophysis. The aim of our study was to examine the relationship between the corticotrophin level and the density, the mobility,

and the percentage of pathological forms of semen as one of indicators of fertilizing ability in a group of men from couples treated for infertility.

Materials and Methods

Human subject

The study was based on results of the examination of 83 men from couples treated for infertility in the Gynecology and Infertility Clinic of the Jagiellonian University in Krakow. All the sampling took place between 9 a.m and 12 noon in the following order: venous blood collecting for hormonal determination followed by semen collecting during masturbation.

The semen was assessed following the criteria of the WHO in the Infertility Laboratory of the Gynecology and Infertility Clinic of the Jagiellonian University in Krakow [7].

Hormone assays

ACTH plasma concentration was assessed in whole blood samples, collected approximetly at o'clock 9 in the morning in silicon-coated glass tubes containing EDTA as an anticoagulant, and were centrifuged immediately in a refrigerated centrifuge. All samples were frozen at –20 °C until the ACTH analysis was performed. Immunoassay was used to measure ACTH. (Immulite 2000 ACTH, DPC Ltd- United States). Determination of FSH, LH, cortisol, testosterone and androstendion was performed using ELISA (Biomerica, USA).

Statistical analysis

Data were compiled in Microsoft Excel 2002 in PC. Statistical analysis was performed with the use of the software Statistica for Windows 5.1M. The distribution of subjects was analyzed with Shapiro-Wilk's test. Differences between average values in particular groups were calculated with the use of variances analysis (ANOVA). For non-parametric data Kruskal-Wallis test was used. Differences between studied groups were considered as significant at $p<0.05$.

Results

The average ACTH level for the whole studied group was 18.58pg/ml (standard deviation 8.62) in the range from 6.06 to 49 pg/ml, so only at lower level it did not fit into the adopted norm (9–52pg/ml). The main group was divided into three subgroups according to ACTH level. Group I – ACTH level <–1, standard deviation adopted between 5–10pg/ml, group II –ACTH level between –1 and +1, standard deviation adopted between 11–30pg/ml, group III – ACTH level > +1, standard deviation adopted between 31–50pg/ml. The characteristics of semen parameters in particular groups are shown in *Table 1*.

The average patients' age ranged from 33.25 to 37.25 years, the average time of sexual abstinence before the examination in group I was 6.6 days as compared to 4.42 and 3.00 in groups II and III respectively. No statistical significance was identified regarding age and sexual abstinence time between examined groups (data not provided in tables). According to the data provided in *Table 1*, the growing ACTH level is related to the drop of semen volume and the mobility of type A sperm cells (progressive fast motion), whereas the number of immobile sperm cells grows. The variances analysis revealed that only the difference in semen volume is statistically significant ($F=5.63$; $p<0.01$). The post-hoc Tukey test established the difference in the volume of semen between group III and groups II and I. Other

Table 1: Semen parameters characteristics (volume, pH, concentration, motility type A and D) in three selected groups

	Group I (N=24)		Group II (N=41)		Group III (N=18)	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	37,25	10,33	33,25	6,88	36,89	5,78
Abstinence (days)	6,6	4,72	4,42	4,23	3,00	1,73
Volume (mL)	4,8	2,11	2,96	1,20	1,73	1,54
pH	7,34	0,09	7,35	0,36	7,73	0,31
Concentration (mln/mL)	32,5	28,30	29,58	22,19	18,67	27,30
Motility type – A (%)	34,25	23,99	25,00	15,24	21,50	9,19
Motility type – D (%)	35,5	18,56	40,10	17,89	58,50	0,71

Table 2: Characteristics (mean, standard deviation –SD) of hormonal plasma concentration (cortisol (µg/mL), LH (mIU/mL), FSH (mIU/mL), testosterone (ng/dL)) in three selected groups

	Group I (N=24)		Group II (N=41)		Group III (N=18)	
	Mean	SD	Mean	SD	Mean	SD
LH (mIU/mL)	3,87	2,82	4,02	2,75	4,84	3,63
FSH (mIU/mL)	4,19	2,22	6,11	7,93	5,71	3,94
Testosterone (ng/dL)	437,13	235,14	486,35	214,47	528,50	277,41
Cortisol (µg/mL)	7,35	4,71	10,34	4,28	16,32	3,31

Table 3: Spearman rank correlation test between ACTH and FSH, LH, cortisol, testosterone, androstendion and between androstendion and testosterone in two groups:
Group 1 – men with sperm concentration > 20mln/ml; Group 2 – men with sperm concentration < 10mln/ml

	Sperm concentration >20mln/mL		Sperm concentration <10mln/mL	
	R Spearman	P	R Spearman	p
ACTH & FSH	-0,26	0,22	0,60	0,03
ACTH & CORTISOL	0,65	0,00	0,80	0,00
ACTH & LH	0,21	0,32	0,71	0,01
ACTH & TESTOSTERON	0,10	0,64	0,13	0,68
ACTH & ANDROSTENDIONE	0,25	0,23	0,69	0,01
ANDROSTENDIONE & TESTOSTERONE	0,42	0,04	0,33	0,29

parameters (including semen pH, sperm cells concentration and mobility) measured were not statistically significant. The average values of obtained hormones levels in examined groups are presented in *Table 2*. The rise of ACTH level is related to the minimal steady growth of LH and testosterone levels (the changes were not statistically significant), whereas FSH level is stable and does not change. On the contrary, the average cortisol level rises and the value ranges from 7.35 μg/mL in group I up to 16.32 μg/mL in group III, and the analysis of variances revealed that the difference was statistically significant (F=9.79; p<0.001).

Discussion

ACTH level in the group of examined men corresponded to with the adopted norm. But the rise of corticotrophin in the range of norm (in groups I, II, III) was related to the decrease of the quality of semen determined by the semen volume, sperm cells concentration and mobility. In groups I and II the drop of determined parameters was still in the range of norm, whereas in group III it was below the level of norm established by the WHO. The average semen volume in group III was 1.73 mL (norm>2mL), sperm cells concentration was 18.67 mln/mL (norm>20.00mln/mL), the average percentage of progressive fast motion sperm cells was 21.50% (norm>25%) and the average percentage of immobile sperm cells was 58.5% (norm<50%). Only the drop of semen volume was statistically significant in our statistical analysis.

As it was assumed in the introduction that the activation of HPA axis should result in the drop of GnRH pulsating secretion, leading to the decrease of gonadotropin hormones level and the drop of testosterone level in consequence causing the arrest of spermatogenesis. Neither the decrease of gonadotropin hormones nor the fall of testosterone level was observed in our current study. The gonadal axis did not seem to be responsible for the drop of semen quality in the group of men observed in the study. A statistically significant rise of ACTH level and/or cortisol in examined groups seemed to be the reason of the decrease of semen volume, sperm cells concentration and their mobility.

M. Fenske [1] applied 20 IU ACTH in adult male guinea pig, measuring the blood serum levels as well as the levels in the tissues of adrenal glands and testis of the following hormones: cortisol, progesterone, androstendion, LH and testosterone. A statistically significant drop of testosterone level was observed which depended on cortisol level. LH level was stable. These results were in compliance with other reports [5,6]. No testosterone drop was observed in animals which were given dexametasone before the ACTH application in spite of cortisol rise. According to this finding, a hypothesis concerning direct cortisol action on Leydig- cells was suggested. Because no differences were found in progesterone level between the group which was administered ACTH and the control group, and androstendion and testosterone levels were high in both groups it was suggested that cortisol might inhibit the testosterone synthesis in guinea pigs distally to progesterone but before androstendion. The administration of dexamethasone down-regulates the glicocoricosteroid receptor in Leydig- cells, which prevents the inhibition of testosterone synthesis.

Our observations might also confirm this hypothesis. The patients were divided into two groups with respect to the quality of semen with sperm cells concentration adopted as a criterion. The first group included 54 men with sperm count >20mln/mL and the second group included 13 men with sperm count <10mln/mL. The levels of ACTH, cortisol, FSH, LH, testosterone and androstendion were compared between these groups. A higher hormones level was identified in the second group, however the differences were not statistically significant. A statistically significant correlation was noticed between ACTH and cortisol levels in group I. The same correlation was found in group II where statistically significant relations were identified between ACTH, gonadotropins and androstendion. In group I a low, statistically insignificant correlation was observed between ACTH and testosterone.

The statistically significant correlation between androstendion and testosterone in the group of patients with normal sperm cells number in the semen is the most important finding supporting the hypothesis of the inhibition of testosterone synthesis in Leydig-cells as the response to ACTH/cortisol rise. In group II lower, statistically insignificant correlation between these

hormones levels was observed (*Table 3*). These results might indicate that the rise of ACTH and cortisol (positive statistically significant correlation in both groups) inhibit the conversion of androstendion into testosterone in Leydig-cells (positive statistically significant correlation in group I and the lack of correlation in group II). As a result, the rise of androstendion and the drop of testosterone synthesis occur. The diminish of reversible inhibition of gonadotropins secretion by testosterone results in the increase of their secretion (positive statistically significant correlation between ACTH and gonadotropins was observed only in group II).

Conclusions

Our results might indicate that the rise of ACTH and cortisol inhibit the conversion of adrostendion into testosteron in Leydig-cells resulting in the rise of androstendion, drop of testosterone production and lower average values of semen volume, sperm cells concentration and A sperm cell mobility and higher value of D sperm cells mobility.

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